Translation

PCT Application
PCT/CN2004/001412

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference OP040073P	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/CN2004/001412	International filing date *(day/month/year)* 03.Dec.2004 (03.12.2004)	(Earliest)Priority date *(day/month/year)* 05.Dec.2003 (05.12.2003)
International Patent Classification (IPC) or national classification and IPC C07D211/90 (2006.01) i		
Applicant SHIJIAZHUANG PHARMACEUTICAL GROUP OUYI PHARMAR, CO., LTD., et al		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 3 sheets, including this cover sheet.

3. This report is also accompanied by ANNEXES, comprising:

   a. ☐ *(sent to the applicant and to the International Bureau)* a total of _____ sheets, as follows:

      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).

      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic _____, containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

   ☒ Box No. I Basis of the report

   ☐ Box No. II Priority

   ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

   ☐ Box No. IV Lack of unity of invention

   ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

   ☐ Box No. VI Certain documents cited

   ☐ Box No. VII Certain defects in the international application

   ☐ Box No. VIII Certain observations on the international application

Date of submission of the demand 30. June. 2005 (30. 06. 2005)	Date of completion of this report 20. Dec. 2005 (20. 12. 2005)
Name and mailing address of the IPEA/CN The State Intellectual Property Office, the P.R.China, 6 Xitucheng Rd., Jimen Bridge, Haidian District, Beijing, China 100088 Facsimile No. 86-10-62019451	Authorized officer Xiao Peng Telephone No. 86-10-62085625

Form PCT/IPEA/409 (cover sheet) (April 2005)

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/CN2004/001412

Box No. I Basis of the report

1. With regard to the **language**, this report is based on:

☒ the international application in the language in which it was filed

☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of:

☐ international search (Rules 12.3(a) and 23.1(b))

☐ publication of the international application (Rule 12.4(a))

☐ international preliminary examination (Rules 55.2(a) and/or 55.3(a))

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☐ the international application as originally filed/furnished

☐ the description:

pages _____ as originally filed/furnished

pages * _____ received by this Authority on _____

pages * _____ received by this Authority on _____

☐ the claims:

pages _____ as originally filed/furnished

pages * _____ as amended (together with any statement)under Article 19

pages * _____ received by this Authority on _____

pages * _____ received by this Authority on _____

☐ the drawings:

pages _____ as originally filed/furnished

pages * _____ received by this Authority on _____

pages * _____ received by this Authority on _____

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/CN2004/001412

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement:

Novelty (N)	Claims	1-12	YES
	Claims		NO
Inventive step (IS)	Claims	1-12	YES
	Claims		NO
Industrial applicability (IA)	Claims	1-12	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

1. Cited Documents

D1: CN1067055C (PFIZ) PFIZER RES & DEV CO NV SA), 13.June.2001, whole document
D2: CN1100038C (Zhang Xitian), 29.Jan.2003, whole document
D3: EP0331315A2 (Pfizer Limited), 06.September.1989, whole document
D4:WO03/035623A1 (Sepracor, INC), 01.May.2003, whole document
D5: US6057344A (Sepracor, INC), 02.May.2000, whole document
D6: Journal of Analytical Science, Vol.19, No.1, Mar., 2003, "Enantiomoeric Separation of Amlodipine by High Performance Capillary Electrophoresis", p33-35

2. Novelty

The methods claimed by claims 1-6 relate to the enantiomoeric separation of optical active amlodipine, which comprising: dissolve the racemic amlodipine and L-(+)-tartaric acid in a solvent containing 2-butone, separate the resulting (S)-(-)-amlodipine-L-(+)-tartaric salt, then subjected to recrystallation in lower alkanol to yield a solid, after which a lower halogenated alkane is added, neutralize with base, finally afford the (S)-(-)-amlodipine.
Documents D1-D6 also disclose methods for the enantiomoeric separation of optical active amlodipine. However, documents D1-D2 use DMSO-d6 or DMSO as solvent, documents D3 and D5 relate to the separation using cinchonidine in methanolic solution, document D4 uses DMAC as solvent, and document D6 relates to the enantiomoeric separation of emlodipine by high performance capillary electrophoresis, thus none of the cited prior art disclose the subject claimed by claims 1-6, and claims 1-6 satisfy the criterion set forth in Article 33(2) and are considered to be novel in respect of the prior art as defined in the regulations (Rule 64 PCT).
Based on the same reason, claims 7-12 also satisfy the criterion set forth in Article 33(2) and are considered to be novel in respect of the prior art as defined in the regulations (Rule 64 PCT).

3. Inventive Step

Documents D1-D2 and D4 are regarded as the closest prior art. However, the use of DMSO and DMSO-d6 as resolution solvents in D1-D2 shows the following disadvantagest: high boiling points and difficulty to recover in the production process, and the use of DMAC as resolution solvents in D4 shows the following disadvantages: high toxicity, high boiling points and being prone to give rise to pollution during the production process. Wheras the method of claim 1-12 use 2-butone as resolution solvent, and thus overcome the above disadvantages.
Although the methods disclosed in D1 and D2 also used 2-butanone, however, the 2-butanone in said methods were used as co-solvent, rather than the solvent for resolution.
Thus, this different selection of the resolution solvent is not obvious to the person skilled in the art, claims 1-12 thus satisfy the criterion set forth in Article 33(3) and are considered to be no obvious in respect of the prior art as defined in the regulations (Rule 65 PCT).

4. Industrial Applicability

The subjects claimed by claims 1-12 of the present invention fulfil the criterion of industrial applicability set forth in Article 33(3) PCT.